REMARKS

Applicants have amended the specification in the manner suggested by the examiner in order to define the acronyms accepted in the field. Without acquiescing in any rejection, applications have canceled claims 1-19 without prejudice or disclaimer and applicants reserve all rights to such subject matter. Applicants have added claims 20-28, which moot the rejections made by the examiner. Support for the new claims is found throughout the specification, particularly at paragraphs 11, 22-27, 37, 54, 55 and 82, and the original claims. Applicants believe that the mootness of the section 101 and indefiniteness rejections is apparent without the need for further discussion. Applicants also provide a certified copy of Austrian priority application A 1872/1998, filed November 10, 1998, which applicants claim priority to. The prior art rejections are discussed below.

The claimed invention is not taught by Eaton, Lollar or Lenting

On pages 5-8 of the office action, the examiner made several anticipation rejections. Applicants respectfully traverse these rejections.

Applicants note that in order to reject a claim under 35 USC § 102, the examiner must demonstrate that each and every claim term is contained in a single prior art reference. *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986); *see also* MPEP § 2131 (August 2001). Claim terms are to be given their plain meaning as understood by the person of ordinary skill in the art,

particularly given the limitations of the English language. *See* MPEP §§ 707.07(g); 2111.01 (August 2001). Claims are to be given their broadest reasonable interpretation consistent with applicants' specification. *See In re Zletz*, 13 USPQ2d 1320, 1322 (Fed Cir. 1989) (holding that claims must be interpreted as broadly as their terms reasonably allow); MPEP § 2111 (Rev. 1, February 2003).

Not only must the claim terms, as reasonably interpreted, be present, an allegedly anticipatory reference must enable the person of ordinary skill to practice the invention as claimed. Otherwise, the invention cannot be said to have been already within the public's possession, which is required for anticipation. *See Akzo, N.V. v. U.S.I.T.C.*, 1 USPQ2d 1241, 1245 (Fed. Cir. 1986); *In re Brown*, 141 USPQ 245, 249 (CCPA 1964). Applicants review below the references with these concepts in mind.

Eaton

The examiner rejected claim 1 as anticipated by Eaton. The examiner did not reject the claims dependent thereon.

According to the examiner, Eaton discloses a factor VIII molecule that lacks the light chain, namely regions A3, C1 and C2. The examiner is incorrect in this characterization, however, because Eaton really lacks a portion of the heavy chain (deletion of residues 797-1562), and therefore does not concern the light chain at all.

Even if the examiner's characterization were correct, then Eaton would disclose a molecule that lacks the entire light chain, namely regions A3, C1 and C2. Applicants invention, however, requires the presence of domain A3 and requires certain

modification(s)[1] in portion(s) of this domain. Given that Eaton would lack all three light chain domains, it cannot meet the claim recitation requiring substitutions in portions of the light chain domains (A3, and C1 or C2 in several other dependent claims). Therefore, an anticipation rejection based upon Eaton cannot be maintained.

Lollar

The examiner rejected claim 1 as anticipated by Lollar. The examiner did not reject the claims dependent thereon.

According to the examiner, Lollar discloses a hybrid protein formed by fusing a human factor VIII heavy chain with a porcine factor VIII light chain. There are no changes in the domains of the porcine light chain *per se*. The claims, however, require certain modifications in portion(s) or one or more of the domains of the light chain. Given that Lollar does not disclose modifications within a light chain domain, it cannot anticipate the claims and therefore a rejection based upon Lollar cannot be maintained.

Lenting

The examiner rejected claim 1 as anticipated by Lenting. The examiner did not reject the claims dependent thereon.

According to the examiner, Lenting discloses the binding of LRP to a factor VIII C2 domain. See figure 5. The claims, however, require certain modifications in

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[1] The modifications can be amino acid substitution (which can be done recombinantly or chemically), addition or deletion.

portion(s) or one or more of the domains of the light chain, and require the presence of light chain domain A3. Given that the C2 domain alone, by definition, lacks the A3 domain, Lenting cannot anticipate the claims. Therefore, a rejection based upon Lenting cannot be maintained.

It should also be noted that Lenting was published in the August 20, 1999 issue of the Journal of Biological Chemistry. The captioned application, however, claims priority to Austrian application serial no. A 1872/98, filed November 10, 1998. Accordingly, Lenting is not prior art.

The claimed invention in not suggested by the combination of Lollar, Lenting and Schwarz

On pages 8-10 of the office action, the examiner rejected claims 1 and 15 as obvious over Lollar, Lenting and Schwarz. Lollar and Lenting were essentially applied as before. Schwarz was cited for disclosing certain benefits associated with von Willebrand Factor and receptor associated protein (RAP). Applicants respectfully traverse this rejection.

At the outset, applicants note that the examiner must show all of the recited claim elements in the combination of references that make up the rejection. When combining references to make out a *prima facie* case of obviousness, the examiner is obliged to show by citation to specific evidence in the cited references that (i) there was a suggestion/motivation to make the combination and (ii) there was a reasonable expectation that the combination would succeed. Both the suggestion/motivation and

reasonable expectation must be found within the prior art, and not be gleaned from applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988); *W.L. Gore v. Garlock, Inc.*, 220 USPQ 303, 312-13 (Fed. Cir. 1983) (holding that is improper in combining references to hold against the inventor what is taught in the inventor's application); *see also* MPEP §§ 2142-43 (Rev. 1, February 2003). Thus, the examiner must provide evidentiary support based upon the contents of the prior art to support all facets of the rejection, rather than just setting forth conclusory statements, subjective beliefs or unknown authority. *See In re Lee*, 277 F.3d 1338, 1343-44 (Fed. Cir. 2002).

When an examiner alleges a *prima facie* case of obviousness, such an allegation can be overcome by showing that (i) there are elements not contained in the references or within the general skill in the art, (ii) the combination is improper (for example, there is a teaching away or no reasonable expectation of success) and/or (iii) objective indicia of patentability exist (for example, unexpected results). *See U.S. v. Adams*, 383 U.S. 39, 51-52 (1966); *Gillette Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ2d 1923, 1927 (Fed. Cir. 1990); *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve*, 230 USPQ 416, 419-20 (Fed. Cir. 1986). The references are discussed with these legal concepts in mind.

The deficiencies of Lollar and Lenting are discussed in detail above. Lollar discloses what amounts to a 'chain swap' between human and porcine factor VIII, yet discloses no modification within a domain of the factor VIII light chain as required by the claims. Moreover, Lenting discloses the use of a C2 domain unaccompanied by the A3 domain. The presence of a modified A3 domain, however, is required by the claims.

Accordingly, the combination of Lollar and Lenting does not teach or suggest a modified factor VIII polypeptide as recited by the claims.

Finally, Schwarz does not rectify the deficiencies of Lollar and Lenting. First, Schwarz does not teach or suggest making a modified factor VIII polypeptide as recited in the claims. Second, with regard to now canceled claim 15, Schwarz does not disclose a composition comprising a modified factor VIII polypeptide with a LRP antagonist, such as RAP. Rather factor VIII and RAP were administered sequentially. See Schwarz at page 1705, column 1 and page 1710, column 2.

It should also be noted that Schwarz was published in the March 2000 edition of Blood, which is after the November 10, 1999 filing date of PCT/AT99/00272. Accordingly, Schwarz, like Lenting discussed above, is not prior art. In view of the above, applicants respectfully submit that the obviousness rejection cannot be maintained.

Request

Applicants submit that the claims are in condition for allowance, and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 912-2000 should there be any questions.

Respectfully submitted,

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